PATENT SPECIFICATION (11) 1 297 221

NO DRAWINGS

(21) Application No. 20315/71 (22) Filed 19 April 1971

(31) Convention Application No. 7004199 (32) Filed 6 Feb. 1970 in

(33) France (FR)

(45) Complete Specification published 22 Nov. 1972

(51) International Classification A61K 9/00

(52) Index at acceptance

A5B 763 766

(54) A MEDICINAL FORM COMPRISING MICROCAPSULES

(71) We, C.R.T. (CENTRE DE RECHERCHE THERAPEUTIQUE), a French Body Corporate, of 58 Rue de la Glacière, Paris 13 ème, France, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to a medicinal form wherein the active therapeutic substance is encapsulated and the microcapsules are in a stable suspension in a liquid vehicle having a density equal to that of the microcapsules.

Microencapsulation is a conventional encasing technique in which powders or liquids are divided into microscopic particles and enclosed in a thin, strong shell which is impermeable to the substance contained. The resulting capsules are presented in the form of a dry, slightly granular powder which ensure the encapsulated products of excellent preservation if they are fragile, the absence of taste if they are not agreeable, and continuous, progressive liberation which is therapeutically valuable in certain cases.

The pharmaceutical form known up to the present time for the administration of microcapsules comprises tablets, which are presented like conventional tablets and are obtained by agglomeration of microcapsules. Although this form is perfectly suitable for adults, it cannot be used for young children or animals.

According to the present invention there is provided a stable homogenous medicinal form for oral administration, comprising a suspension of microcapsules in a gelified excipient having a density equal to that of said microcapsules, said microcapsules containing at least one therapeutically active substance inside a wall soluble in a body juice and inert in relation to said active substance and insoluble in said excipient.

The excipient may be an aqueous solution containing at least one gelling agent for example an aqueous gel of guar gum and pectin.

This form of medicine can be presented as a thick liquid or as a jelly or "jam" in which the taste of the active substance is completely masked. It is therefore particularly suitable for children, to whom it can very simply be given, for example in a teaspoon, and for animals, to which it may be administered just as it is or else for example by mixing it with their feed, or with the aid of a syringe. In addition to a simplified form of administration and the absence of an unpleasant taste, this medicinal form has beneficial therapeutical effects. The liberation of the active substance through the dissolving of the wall of the microcapsules in the alimentary tract or in a body liquid is continuous, progressive, and regular. Moreover, the jelly form is particularly advantageous in the case of gastro-intestinal affections, because so to speak it applies a dressing to the mucous membranes.

This form of medicine is administered in the usual medicinal dose for the active substance encapsulated.

Examples of encapsulatable substances are diuretics, cardiovascular agent, analgesics, sedatives, antiallergics, antibiotics, enzymes, and vitamins.

According to the invention the wall of the microcapsules must be insoluble in the liquid excipient serving as vehicle for the microcapsules and soluble in the juices of the organism, digestive or other system, in order to liberate the imprisoned active substance. In addition, it must be inert in relation to the encapsulated substance. This wall may advantageously be of ethyl cellulose, which is soluble in the juices of the digestive system.

The excipient may be of a gelatinous consistency and may for example be composed of an aqueous gel of guar gum, gelatine, pectin, agar-agar, alginates, carragheenates, or any other substances capable of holding the grains in suspension.

This excipient may contain one or more preservative agents normally used in pharmacy, such as methyl or propyl p-hydroxybenzoate. It may in addition contain sugar, aromatics,

or flavourings to give an agreeable taste to the medicine. It may also contain one or more other active substances.

Numerous conventional processes are known for the preparation of microcapsules. These processes may use techniques as diverse as coating, extrusion, or formation *in situ* in emulsion. These processes, and also examples of materials used for forming the walls, are described in particular in the U.S. patents 2,730,456, 2,730,457, 2,800,457, 2,969,330, 3,041,288; 3,111,407, 3,116,206, and 3,173,878.

The microcapsules which are prepared in this manner, and which have a diameter of 20 to 150 microns, are suspended in a semi-liquid vehicle having a density equal to that of the capsules. The nature and amounts of the components of the vehicle depend on the amount and the weight of the microcapsules and also on the nature of their shell and of the vehicle, as well as on the dimensions of the microcapsules.

A medicinal form of the invention may contain microcapsules of different therapeutical substances.

The invention will be better understood on reading the following detailed description of a non-limitative example of an embodiment of the invention.

Example

Tetracycline hydrochloride microcapsules having an ethyl cellulose wall are prepared by a conventional process.

For 50 g of tetracycline hydrochloride microcapsules an excipient having the following composition is used:

Pectin	14.05 g
Guar gum	0.95 g
Sugar	468.50 g
Crystal glucose	168.50 g
Citric acid	0.95 g
Flavouring	13 g
Methyl parahydroxybenzoate	0.90 g
Propyl parahydroxybenzoate	0.45 g
Water to make	950 g

425 ml of water containing the citric acid and the preserving agents is brought to boiling point. The pectin, guar gum, and part of the sugar are added and mixed until homogeneity is achieved. The remainder of the sugar is added while the mixture is still boiling. The mixture is allowed to cool. The weight obtained must be 937 g.

The mixture is left to stand for 24 hours so as to obtain a stable gelled solution.

Finally, the tetracycline microcapsules and the flavouring are added.

This medicine is in the form of a jelly. It can be administered in spoonfuls to children in the usual medicinal dose for tetracycline, that is to say 1 to 2 g per day. The only taste of this medicine is that of the excipient and not that of the active substance.

WHAT WE CLAIM IS:—

1. A stable homogenous medicinal form for oral administration, comprising a suspension of microcapsules in a gelified excipient having a density equal to that of said microcapsules, said microcapsules containing at least one therapeutically active substance inside a wall soluble in a body juice and inert in relation to said active substance and insoluble in said excipient.

2. A medicinal form according to claim 1, wherein the excipient is an aqueous solution containing at least one gelling agent.

3. A medicinal form according to claim 2, wherein the excipient is an aqueous gel of guar gum and pectin.

4. A medicinal form according to any one of claims 1, 2 or 3, wherein the excipient contains at least one preserving agent.

5. A medicinal form according to claim 1 comprising a suspension of tetracycline hydrochloride microcapsules, having an ethyl cellulose wall suspended in a gelified aqueous solution containing guar gum and pectin.

6. A medicinal form according to claim 1 substantially as described with reference to the specific example hereinbefore set forth.

REID CLARKE & CO.,
Chartered Patent Agents,
Agents for the Applicants,
Craven House, 121 Kingsway,
London, WC2B 6PJ.

Printed for Her Majesty's Stationery Office, by the Courier Press, Leamington Spa, 1972.
Published by The Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.